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Outpatient Management of Fever in Children With Sickle Cell Disease (SCD) in an African Setting

Mohamed Cherif Rahimy,[1]* Annick Gangbo,[1] Gilbert Ahouignan,[1] Severin Anagonou,[2] Vicencia Boco,[3] and Eusebe Alihonou[1]

[1]Newborn Screening for Sickle Cell Disease and Comprehensive Clinical Care Programs Health Sciences Faculty, Cotonou, National University of Republic of Benin (West Africa)

[2]Unit of Bacteriology and Virology Health Sciences Faculty, Cotonou, National University of Republic of Benin (West Africa)

[3]Unit of Radiology, Health Sciences Faculty, Cotonou, National University of Republic of Benin (West Africa)

Because hospitalization and intravenous antibiotics for treatment of a potentially fatal bacterial infection in febrile children with sickle cell disease (SCD) are difficult to apply, outpatient treatment has been considered in developed countries for selected patients. Eligibility criteria and procedures may differ in developing countries because of unique economic and social conditions. After clinical evaluation within 36 hr of the onset of a fever exceeding 38.5°C, children with SCD who are being closely followed as a part of a SCD cohort in Cotonou (West Africa), were treated as outpatients. The antibiotic regimen consisted of intramuscular injection of ceftriaxone 50 mg/kg/day for 2 days followed by amoxicillin 25 mg/kg × 3/day × 4 days and oral hyper-hydration. Patients were observed for 6 hr and thereafter discharged with a medical control at day 2, day 8 + day 15. All 60 children included completed their treatment, and none were lost to follow-up. A definite or a presumed bacterial infection was the cause of the febrile episode in 76.7% of cases. An appreciable decrease in fever was observed from day 2 and only 2 patients were hospitalized at day 3, one for abdominal painful crisis and one other for persistent fever without documented infection. No severe bacterial infections, recurrence of febrile episode, nor death were encountered during the follow-up. The cost of this outpatient approach is US $30 per patient as compared to US $140 per patient if the patient had been hospitalized. Outpatient management of febrile episode in children with SCD is feasible and cost-effective in Sub-Saharan African. It requires, however, improved medical education on SCD and immediate medical attention after the onset of fever. Am. J. Hematol. 62:1–6, 1999.

Key words: Sickle cell disease; bacterial infections; fever; antibiotic therapy; child

INTRODUCTION

Despite the use of prophylactic oral penicillin and specific vaccinations, bacterial infections remain one of the major causes of death in children with sickle cell disease (SCD). Thus hospitalization and prompt administration of an intravenous antibiotic regimen is the recommended approach for the management of febrile episodes in infants with SCD [1,2]. Bacterial infection is one of the most frequent events encountered during early childhood in children with SCD [3–7], however, implementation of this approach in an African setting is difficult. Repeated hospitalizations with a disruption of home life may psychologically affect the child and result in considerable expenditure of health care resources. Parents are often unwilling to hospitalize their children, and overcrowding of hospitals is common. Thus, this conservative approach is unlikely to be applied in areas with high prevalence of sickle cell disease, because of lack of medical education

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*Correspondence to: Dr. M.C. Rahimy, P.O. 01 Box 2640 RP Cotonou Rep of Benin (West Africa). E-mail: mrahimy@syfed.bj.refer.org

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and inadequate health care facilities. Recently, with the availability of newer antibiotics that provide effective coverage against the principal microbes involved in such infections (i.e., *Streptococcus pneumoniae, Salmonella species, Haemophilus influenzae* type b) and that have similar prolonged serum half-lives [8,9], outpatient therapy has been considered. Preliminary results from developed countries suggest that it could be a safe and cost-effective approach for selected patients [9–11]. However, eligibility criteria and procedures used in industrialized countries might be irrelevant in sub-Saharan countries: often, there are no dedicated sickle cell clinics, and children with SCD are not followed; patients frequently present several days after onset of symptoms; possibility of laboratory analyses is restricted; and the required above-mentioned antibiotics are not always affordable.

Likewise, in our country, there are no dedicated sickle cell centers and children with SCD are not followed up. Recently, a Neonatal Screening Program for SCD and a Comprehensive Clinical Care Program were setup in Cotonou, the economic capital city of Benin, a West African country. We have conducted an open and nonrandomized prospective clinical trial aimed at estimating the feasibility and efficacy of outpatient management of febrile episodes in children with SCD participating in the above-mentioned programs.

METHODS

Patient Population

The patients were children from a Neonatal Screening Program for SCD and a Comprehensive Clinical Care Program which were both initiated in May 1993. A special clinic within the National Teaching Hospital has been allocated to the programs for their clinical activities: follow-up medical visits, parental education, emergency visits, specific treatment, etc. Clinical management is partly based on repeated parental information, training and education sessions on SCD, twice daily oral penicillin for pneumococcal infection prophylaxis and chloroquine every second day for *Plasmodium falciparum* malaria *prophylaxis*. The educational themes emphasize that febrile episodes require immediate attention at the designated SCD clinic. Pneumococcal and *Haemophilus influenzae* type b vaccines are strongly recommended and offered at a low cost.

Study Design and Procedure

This study was an open and prospective clinical trial carried out from January 1, 1995 to December 31, 1996. Inclusion criteria were presentation at the SCD clinic within 36 hr of the onset of a fever exceeding 38.5°C without previous antibiotic treatment other than oral penicillin. Patients were excluded when they had any of the following features: serious ill appearance with hypotension and poor peripheral perfusion (capillary-refill time > 4 sec), severe painful crisis, dehydration, osteomyelitis, sign of respiratory distress, sign of neurological involvement or chest X-ray showing infiltration of a large portion of the lungs. Patients with a past history of allergy to cephalosporin were also excluded. Parents gave informed consent for the study, which was approved by the Ethics committee of the Faculty of Health Sciences.

All patients were examined, observed and followed by the same investigator. The antibiotic regimen consisted of intramuscular injection of ceftriaxone 50 mg/kg/day × 2 days followed by amoxicillin 25 mg/kg × 3/day × 4 days and oral hyper-hydration. Medical follow-up was performed at day 2, day 8 and day 15 at the SCD clinic. Eligible patients received their first ceftriaxone injection immediately after physical examination and sampling for blood cultures. They were given paracetamol as antipyretic therapy. Patients were observed for 6 hr and then discharged. Oral quinine to treat for malaria was added if necessary. Antibiotics were donated by the Fondation Roche de Recherche en Afrique.

Laboratory tests included: complete blood count at day 1 and day 8; blood cultures (twice) urine culture, blood smears for *Plasmodium falciparum* asexual parasites count, and chest X-ray at day 1, repeated day 15 if abnormal. Sera were frozen and stored at −20°C at day 1 and day 8 for subsequent measurement of C-reactive protein and orosomucoid levels.

C-reactive protein and orosomucoid levels were measured at the Laboratoire de Biochimie Medicale, Institut Pasteur (Abidjan, Ivory Coast). For the first consecutive 38 patients, serum C-reactive protein levels were measured in duplicate at the Department de Biologie Clinique, Institut Gustave Roussy (Cedex, France). No discrepancy was found between results of the two laboratories.

Data Analysis

The primary variables of interest were the number of hospitalizations required during the three-day period following inclusion and the frequency and feature of documented bacterial infection (i.e., septicemia, meningitis, osteomyelitis, and pneumonia) occurring within the 8 day period after inclusion. Also considered were the recurrence of another febrile episode and/or the occurrence of other sickle cell-related events within the following 2 weeks. The neutrophil leukocytes (NL) count; C-reactive protein level and orosomucoid level at day 1 were compared to their values at day 8. As white blood cell count and temperature have been described as possible indicators of bacteremia in childhood [12], we presumed that a patient had had a bacterial infection when a significantly elevated NL count was observed at day 1 as compared to steady state level, and a NL count at day 1/NL count at

TABLE I. Patients' Characteristics at Admission and their Clinical Evolution*

Characteristics	Value
Number of patients	60
Age (months)	
Median	23.7
Range	6–138
Below 60 months (number)	48
Hemoglobin phenotype	
SS (number)	56
SC (number)	4
Sex	
Male (number)	40
Female (number)	20
Temperature at admission (mean ± SD)	39.4 ± 0.4°C
Temperature at day 2 (mean ± SD)	37.9 ± 0.8°C
Hospitalization required (number)	2
Number of patients transfused	4

*Patients 14, 27, 31, 49 in Tables III–V. No severe bacterial infection, no recurrence of febrile episode and no death were recorded during follow-up.

day 8 ratio greater than 2, in the absence of a definite bacterial infection. Comparisons between group were performed by using Fisher's exact test.

The Comprehensive Clinical Care Program is still a pilot study. Therefore, the vast majority of children with SCD in our country remain without follow-up and specific medical care. Most often, they present at pediatric ward with symptoms lasting for several days and are hospitalized as emergency cases. The routine inpatient management of these patients is not standardized and parents must pay for the treatment of their child. To evaluate the cost effectiveness of outpatient management linked to the comprehensive clinical care program, we considered the mean duration of stay of children with SCD without previous follow-up, hospitalized in pediatric ward for fever or infection as emergency cases during the same period, and compared the cost of this stay (hospitalization and medications) to the cost of the outpatient treatment.

RESULTS

Sixty-one patients were included during the period of study. No parent declined to participate. One infant was immediately withdrawn because blood smears showed 1.20×10^6 *Plasmodium falciparum* asexual parasites/μl, (i.e., more than 30% parasitemia). For this patient (SS homozygote, 6 months old), the parents had disrupted malaria prophylaxis for 3 weeks to fulfill some religious requirements. No child of our cohort evaluated within 36 hr of the onset of a fever exceeding 38.5°C presented with exclusion criteria. All the included children completed their treatment and none were lost to follow-up. Thus, 60 patients were analyzed. Table I lists their characteristics and their clinical evolution. Eighty percent of the patients were below the age of 5 years. An appreciable decrease in fever was observed from day 2 and only 2 patients were hospitalized at day 3 (patient 2 and patient 27). The first was hospitalized for an abdominal painful crisis; he was discharged at day 5. The other was hospitalized for persistent fever without documentation of any infection; he was transfused at day 6 and discharged at day 13. No severe bacterial infection, no recurrence of febrile episode and no death were encountered during the follow-up.

TABLE II. Etiology of the Fever

Etiology	No (%)
Septicemia*	8 (13.3)
Without focal involvement	2
With pneumonia	6
Pneumonia	12 (20.0)
Presumed bacterial infection	26 (43.3)
Plasmodium falciparum malaria	4 (6.7)
Unknown cause	10 (16.7)

*With the *Salmonella* species (3 cases), *Staphylococcus aureus* (3 cases), *Acinetobacter* (1 case), and *Enterobacter* (1 case).

Causes of the febrile episodes were separated into five classes (Table II). Eight patients had septicemia (both blood cultures were positive for identical pathogens) with the *Salmonella* species (3 cases), *Staphylococcus aureus* (3 cases), *Acinetobacter* (1 case) and *Enterobacter* (1 case). Eighteen patients had bacterial pneumonia, which was associated with septicemia in 6 cases. Twenty-six patients had a presumed bacterial infection, and four had *Plasmodium falciparum* malaria. In ten cases, the cause of the fever could not be determined.

Table III lists characteristics of patients with septicemia and/or pneumonia. Six out of these 20 patients (patients 1, 14, 28, 31, 49, 52) had a fever exceeding 38.5°C at day 2; all were afebrile by day 3. Because the children with septicemia were well by the time the results of admission blood cultures were received, no changes were made in treatment. Patients 14 and 49 were transfused at day 2 and patient 31 at day 8, the latter for an aplastic crisis. Within this group, 15 children out of 20 (i.e., 75%) had a high level of CRP at day 1. In patients with initial high level of CRP a dramatic decrease was noticed by day 8 except in 3 cases. Levels of orosomucoid were also elevated at day 1, but changes at day 8 were not obvious as were changes in CRP levels.

The characteristics of the 26 patients defined as having a presumed bacterial infection are listed in Table IV. Like the group of patients with definite bacterial infection, 19 out of 25 patients (i.e., 76%) within this group had a high level of CRP at day 1, and a remarkable decrease in CRP was observed at day 8. All but one had an appreciable decrease in fever from day 2; this one patient had the highest initial level of CRP.

The characteristics of the 10 patients for whom no bacterial origin could be presumed for the febrile episode

TABLE III. Neutrophil Leukocytes Count Day 1/Day 8 Ratio, Hemoglobin Level at Day 1 and Day 8, CRP and Orosomucoid Levels at Day 1 and Day 8 in Patients With Definite Bacterial Infections*

		Temperature (°C)		Ratio NL	Hb (g/dl)		CRP (mg/l)		Orosomucoid (g/l)		
Patient	Phenotype	Day 1	Day 2	Day 1/Day 8	Day 1	Day 8	Day 1	Day 8	Day 1	Day 8	Etiology
1	SS	39.2	39.9	3.8	6.5	6.3	25.0	2.6	2.54	1.26	Septicemia + Pneumonis[b]
3	SS	39.1	37	2.3	7.1	8.2	35.0	2.6	2.13	1.26	Septicemia[b]
4	SS	39.5	37	2.8	8.9	10.0	10.1	2.6	UV	UV	Septicemia + Pneumonia[b]
5	SS	40	37.2	2.5	6.2	9.0	16.3	2.6	UV	UV	Septicemia + Pneumonia[b]
10	SS	39	37.5	3.9	7.4	7.8	20.0	2.6	1.32	0.77	Pneumonia
11	SC	39.2	37.5	2.5	10.0	10.0	26.0	18.1	1.6	1.19	Septicemia + Pneumonia[b]
12	SS	38.7	37.1	3.3	7.5	7.0	16.0	4.3	1.19	1.53	Septicemia[b]
14	SS	39.3	39.3	2.4	4.1	7.7[a]	10.0	4.3	2.63	UV	Septicemia + Pneumonia[b]
15	SS	39.5	38.5	7.3	9.0	9.0	24.0	21.0	2.29	1.89	Pneumonia
19	SS	39.5	37.8	1.9	5.0	5.0	64.0	13.3	2.46	2.21	Pneumonia
20	SS	38.8	37.6	2.9	5.0	5.6	56.0	2.6	2.13	2.63	Pneumonia
28	SS	40	38.8	3.0	6.8	5.3	16.6	4.3	0.055	UV	Septicemia + Pneumonia[b]
31	SS	39.2	39.6	4.4	6.4	3.7[a]	30.1	25.0	UV	UV	Pneumonia
32	SS	40	37.2	2.5	7.5	8.6	24.0	2.6	2.13	1.53	Pneumonia
37	SS	39.5	37.2	4.0	5.4	7.0	6.0	4.3	0.77	UV	Pneumonia
49	SS	39.9	39	6.6	5.3	5.2[a]	67.0	5.0	1.67	2.37	Pneumonia
51	SS	39.5	38	2.9	8.5	9.0	6.0	4.3	1.82	1.6	Pneumonia
52	SS	39	38.9	4.9	6.0	7.0	9.0	4.3	2.05	1.13	Pneumonia
53	SC	39.5	38.3	4.0	8.7	8	6.0	5.0	1.32	1.4	Pneumonia
54	SS	39.2	38	2.7	6.4	8.6	6.0	4.3	2.21	2.05	Pneumonia

*NL, neutrophils leukocytes; UV, unavailable values. CRP normal value described in children with SCD at steady state < 6 mg/l; orosomucoid value described in children with SCD at their steady state < 0.87 g/l [17].

[a]Patients transfused.

[b]Pathogens recovered from blood cultures: *Salmonella paratyphi* A (patients 1, 28); *Salmonella typhi* (patient 5); *Staphylococcus aureus* (patients 4, 11 and 14); *Enterobacter* (patient 3); *Acinetobacter* (patient 12).

are listed in Table V. Unlike the 2 preceding groups, only 3 patients (patients 25, 58, 61) within this group had a high level of CRP at day 1. The comparison with the group of patients with presumed bacterial infections shows that an initial high level of CRP was associated with a significantly elevated NL count at day 1 ($p = 0.01$), suggestive of a bacterial infection.

In four patients, *Plasmodium falciparum* malaria was the cause of fever. Clinical features were always mild and never required transfusion.

While this study was being carried out, one hundred and one febrile children with SCD (SS homozygous) presented at pediatric ward with symptoms lasting for 4–8 days and were hospitalized as emergency cases. Among them, 12 deaths were recorded. The length of the hospital stay was 15 days on average and its cost was partly charged to the parents (approximately US $140 per episode). The outpatient treatment would cost on average US $30 per episode to parents, if not provided free of charge. Thus outpatient care would save parents a mean of US $110 per febrile episode.

DISCUSSION

We have conducted a protocol to evaluate the outpatient management of febrile episodes in children with SCD in Cotonou, the largest city of the Republic of Benin. To the best of our knowledge, this is the first prospective and homogeneous study considering outpatient management of febrile episodes in children with SCD in Sub-Saharan Africa where prevalence of SCD is at its highest. Our results demonstrate the feasibility and the efficacy of such an approach in a developing countries despite limited laboratory resources. We were initially concerned that irrational concepts of SCD due to the social and cultural backgrounds of the population might alter both consent and compliance. But all of the parents brought their children for the second injection of ceftriaxone, and no children were lost to follow-up during the study. This conclusively demonstrates the efficacy of parental education, leading to a better understanding and cooperation.

Bacterial infections are the most common cause of death in children with SCD [3,13]. this may be of a particular importance in our area where over 50% of affected children will not reach their 5th birthday. In Sub-Saharan Africa, a hyper-endemic area of *Plasmodium falciparum* infection, all febrile children are first considered as having malaria (regardless of whether or not they were receiving malaria prophylaxis) and treated accordingly for at least 3 days (WHO recommendations). In this study, we found that 76.7% (46 of 60) of febrile children with SCD actually had a bacterial infection and only 6.7% (4 of 60) had *Plasmodium falciparum* malaria. Thus, to follow the WHO recommendations might be deleterious for children with SCD. As recommended

TABLE IV. Neutrophil Leukocytes Count Day 1/Day 8 Ratio, Hemoglobin Level at Day 1 and Day 8, CRP and Orosomucoid Levels at Day 1 and Day 8 in Patients Presumed to Have Bacterial Infections*

		Temperature (°C)		Ratio NL	Hb (g/dl)		CRP (mg/l)		Orosomucoid (g/l)	
Patient	Phenotype	Day 1	Day 2	Day 1/Day 8	Day 1	Day 8	Day 1	Day 8	Day 1	Day 8
2[a]	SS	395	37.2	2.7	8.3	8.4	22.4	4.3	1.46	2.29
7	SS	39.5	38.6	5.9	7.1	8.4	35.0	2.6	2.89	UV
8	SS	39.0	37.6	5.1	6.1	5.5	11.6	2.6	0.88	UV
9	SS	39.1	37.6	2.6	7.1	6.9	6.0	6.5	0.45	UV
16	SS	39.5	37.5	2.7	8.1	8.6	56.0	4.3	2.17	1.19
17	SS	39.2	39.8	3.5	7.7	8.3	156.0	4.3	UV	UV
18	SS	39.2	37.3	4.5	4.5	5.6	104.0	2.6	2.29	1.97
21	SS	39.7	37.5	4.3	10.2	11.2	20.0	2.6	2.21	UV
26	SS	39.1	37.2	3.9	9.3	8.2	22.8	4.3	UV	UV
29	SS	39.0	38.2	4.7	11.5	10.7	47.0	2.6	2.13	UV
33	SS	40.2	37.0	5.4	7.7	7.1	51.0	4.3	1.26	UV
34	SS	39.5	37.3	3.6	7.7	9.0	10.0	4.3	2.75	1.13
36	SS	39.2	37.8	3.7	8.9	8.8	66.0	4.3	2.80	UV
38	SS	40	38.2	6.3	6.1	7.5	59.0	4.3	1.60	1.13
41	SS	39.5	37.2	3.6	8.0	6.7	4.3	4.3	2.98	2.21
42	SS	40.1	36.9	3.8	9.5	9.0	50.0	4.3	2.63	2.05
43	SS	39.5	38.6	5.0	6.2	7.2	78.0	4.3	2.29	UV
44	SS	39.5	37.2	2.6	7.2	7.5	8.0	4.3	1.89	1.32
45	SS	39.5	37.4	2.4	8.5	7.8	6.0	5.0	1.74	1.82
46	SC	39.5	36.7	7.2	7.6	8.4	6.0	9.0	0.88	0.82
55	SS	39	37.2	6.2	5.5	7.8	30.0	4.3	2.18	1.53
56	SS	39.8	37.3	6.2	5.4	6.8	UV	UV	UV	UV
57	SC	39.2	38.2	11.4	9.6	9.0	6.0	4.3	0.71	0.82
60	SS	40.0	38.2	3.4	6.6	6.9	63.0	5.0	1.53	2.13
62	SS	39.7	37.5	10.0	9.6	8.9	70.0	4.3	1.82	1.67
63	SS	40.2	38.2	3.4	8.2	7.8	26.0	6.0	1.67	2.29

*NL, neutrophils leukocytes; UV, unavailable values.
[a]Patient hospitalized at day 3 for abdominal painful crisis; he was discharged at day 5.

TABLE V. Neutrophil Leukocytes Count Day 1/Day 8 Ratio, Hemoglobin Level at Day 1 and Day 8, CRP and Orosomucoid Levels at Day 1 and Day 8 in Patients of Whom the Cause of the Febrile Episode Could Not Be Determined*

		Temperature (°C)		Ratio NL	Hb (g/dl)		CRP (mg/l)		Orosomucoid (g/l)	
Patient	Phenotype	Day 1	Day 2	Day 1/Day 8	Day 1	Day 8	Day 1	Day 8	Day 1	Day 8
6	SS	38.9	37	0.77	9.3	10.7	2.6	2.6	UV	UV
25	SS	39.2	39	0.70	8.5	6.3	12.1	2.8	0.063	UV
27[a]	SS	40	38.1	1.12	6.5	7.0	4.3	4.3	0.017	UV
35	SS	39.6	37.5	0.60	8.4	6.0	4.7	4.3	1.52	1.46
39	SS	40	38.2	0.75	8.3	8.0	6.0	4.3	1.67	1.53
40	SS	39.2	38	0.73	7.0	7.5	4.3	4.3	1.37	1.46
47	SS	39.3	38.2	0.77	7.7	10.9	UV	UV	UV	UV
58	SS	39	38	0.52	7.0	6.8	69.0	33.0	1.53	1.82
59	SS	39.2	37.4	1.04	9.6	10.0	6.0	4.3	1.19	1.13
61	SS	39.7	36.6	1.20	8.5	7.2	42.0	6.0	1.82	3.95

*NL, neutrophils leukocytes; UV, unavailable values.
[a]Patient hospitalized at day 3 for persistent fever without documentation of any bacterial infection; he was transfused at day 6 and discharged at day 13.

elsewhere, all febrile children with SCD must quickly receive parenteral antibiotics to prevent a potentially fatal bacterial infection. Furthermore, no children seen within 36 hr of the onset of a fever exceeding 38.5°C were too severely ill to be excluded from the study; a rapid visit to the SCD clinic appears, therefore, to be an important prognostic factor in the outcome of bacterial infections in children with SCD.

The identification of pathogens in pneumonia is very difficult, particularly in children from whom sputum culture is difficult to obtain. We were not able to identify precisely the pathogens in the 12 cases of clinically clear-cut bacterial pneumonia, but 6 out of the 8 septicemia cases were associated with pneumonia despite early medical intervention, reflecting the frequency of pulmonary involvement during bacterial infection in children with SCD [14].

Streptococcus pneumoniae was formerly the most frequent agent causing bacterial infection in children with SCD with a high case fatality rate [3,5–7,15]; its effective prevention has been associated with an increasing frequency of other pathogens, especially with Salmonella and *Haemophilus influenzae* type b [16]. *S. pneumoniae* was not present among the pathogens recovered from blood cultures during the present study and no death was recorded; this was probably the result of the effectiveness of the prevention of pneumococcal infection in our cohort.

Several biological markers are currently used in developed countries to differentiate between bacterial and non-bacterial infections in the absence of definite documentation. The subsequent comparison of C-reactive protein levels between time-paired samples (day 1 and day 8) showed a prompt rise in patients with definite or presumed bacterial infection. With antibiotic treatment, this marker concentration lowered rapidly. Due to its biological characteristics (late increase and prolonged half life compared to CRP), changes in orosomucoid level between day 1 and day 8, did not appear obvious. However, in some patients with an initial elevated level, of this biological marker of infection/inflammation, a decrease was observed at day 8. These results, a posteriori, support our definition of the presumed bacterial infection group.

Unlike the intravenous injection most often used in developed countries [9,10], in the present study, the ceftriaxone was given intramuscularly. Ceftriaxone is one of the newer antibiotics that provide effective coverage against the principal microbes involved in bacterial infections in children with SCD. Although a third blood culture was not performed after the second dose of ceftriaxone, the fact that children with septicemia made a complete and uneventful recovery suggested that the two intramuscular injections of ceftriaxone were effective in sterilizing blood and in preventing other focal involvement (including the case of septicemia with *Acinetobacter*, a pathogen that is usually resistant).

Despite the difficulty of initial laboratory assessment in our context, the strategy has permitted over 96% of febrile children with SCD to be completely managed as outpatients. In a context of overall extreme poverty, the associated savings were considerable; the Annual Gross Domestic Product of Benin was estimated at US $287 (1994) while outpatient management of febrile children with SCD as compared to hospitalized patients saved as much as US $110 per episode. Thus, outpatient management of febrile episodes in children with SCD is feasible in Sub-Saharan Africa; however; the prerequisites before implementation of this approach include: i) improved medical education, especially on SCD; ii) ability to closely monitor children treated with outpatient care; iii) immediate medical attention following onset of fever; and iv) availability of antibiotics that provide effective coverage against principal microbes involved in bacterial infections in children with SCD.

Although the present study is now concluded, we continue to manage febrile episodes in children with SCD from our cohort with outpatient care, provided a rapid clinical evaluation can be performed. Interestingly, the parents consent to buy the ceftriaxone.

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